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Health and Environmental Effects Profile fo Dalapon

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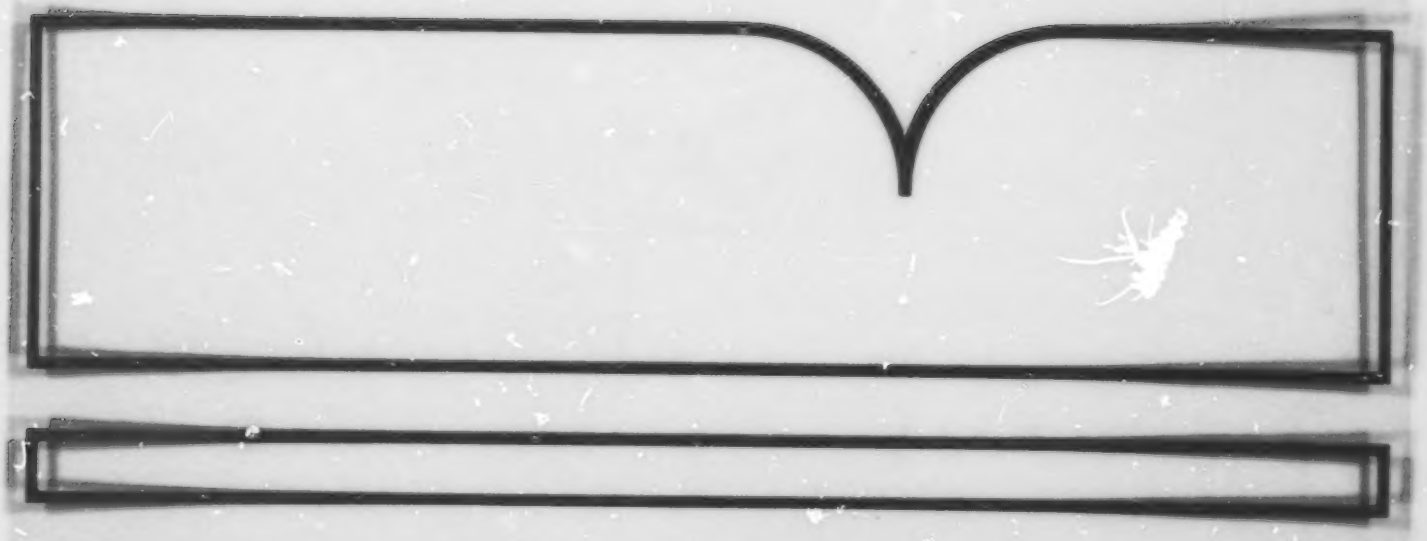

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR DALAPON

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT

The Health and Environmental Effects Profile for dalapon was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Dalapon has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for dalapon is 8.5×10^{-2} (mg/kg bw/day) for oral exposure.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficiemt data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

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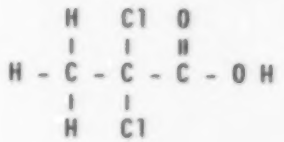
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
BOD	Biochemical oxygen demand
bw	Body weight
LC_{50}	Concentration lethal to 50% of recipients (and all other subscripted dosage levels)
LD_{50}	Dose lethal to 50% of recipients (and all other subscripted dosage levels)
LOEL	Lowest-observed-effect level
LT_{50}	Time lethal to 50% of recipients (and all other subscripted dosage levels)
NOEL	No-observed-effect level
ppb	Parts per billion
ppm	Parts per million
RNA	Ribonucleic acid
TLV	Threshold limit value
TWA	Time-weighted average

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Dalapon is the common name for 2,2-dichloropropionic acid. The sodium salt of dalapon was introduced as a herbicide in 1953 by the Dow Chemical Company under the trademarks "Dowpon" and Radapon" (BCPC, 1977). Other chemical synonyms and trade names for dalapon include alpha-dichloropropionic acid, Basfapon, Basinex, Crisapon, Ded-Weed, Gramevin, Kenapon, Liropon, Proprop and Unipon. The structural formula for dalapon is:



The empiracal formula and molecular weights of dalapon and its commercial salts are listed in Table 1-1 along with the Chemical Abstract Service (CAS) numbers.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Dalapon is available commercially as a formulation of the sodium and magnesium salts. The formulations available are as follows (WSSA, 1979):

Dowpon	the sodium salt of dalapon
Radapon	a liquid formation of the sodium salt
Dowpon M	a mixture of the sodium salt of dalapon (72.5%), the magnesium salt of dalapon (12.0%) and inert ingredients (15.5%) (Kenaga, 1974)

Selected physical properties of dalapon, its sodium and magnesium salts and Dowpon M are listed in Table 1-1.

TABLE 1-1

Physical Properties of Dalapon and Its Salts*

Property	Dalapon	Dalapon Sodium Salt	Dalapon Magnesium Salt	Dowpon M
Molecular weight	143	165	308.5	NA
Empirical formula	$C_3H_4Cl_2O_2$	$C_3H_3Cl_2NaO_2$	$C_6H_6Cl_4MgO_4$	NA
Physical state	liquid	solid	solid	solid
Color	colorless	white	white-tan	off-white
Density	1.389 (22.8°C)	NA	62.5 lb/cu.ft.	NA
Melting point	20°C	decomposes (193-197°C)	decomposes (193°C)	decomposes
Boiling point	185-190°C	NA	NA	NA
CAS numbers	75-99-0	127-20-8	NA	NA
Octanol/water partition coefficient	5.7	<1	NA	NA
Solubility(g/100 g solvent, 25°C)				
Water	>80	90	780	110 g/100 mℓ (22°C)
Acetone	NA	0.14	NA	NA
Methanol	18.5	17.9	35.9	NA
Ethanol	82.7	<18.5	25.5	NA
Benzene	NA	0.002	4.4	NA
Ether	sol.	0.016	NA	NA
Kerosene	NA	NA	0.055	NA
Ionization constant in water, K_a	2.94×10^{-2}	NA	NA	NA
Log octanol/water partition coefficient (Hansch and Leo, 1981)	0.78	NA	NA	NA

*Sources: WSSA, 1979; BCPC, 1977; Kenaga, 1974

NA = Not available

The sodium salt of dalapon hydrolyzes slowly at 25°C, but the hydrolysis becomes comparatively rapid at ≥50°C; aqueous solutions should not be kept for any length of time (BCPC, 1977). Above 120°C, alkali causes dehydrochlorination. Solutions are corrosive to iron.

1.3. PRODUCTION DATA

Dalapon is formed by the chlorination of propionic acid (BCPC, 1977). The sole domestic producer of dalapon is Dow Chemical in Midland, MI (SRI, 1983). Current production figures are not published; however, based on the consumption use of dalapon's precursor, propionic acid (CMR, 1982), ~10-20 million pounds of dalapon are estimated to be produced annually. In 1975, a reported 5.7 million pounds of dalapon were used domestically (SRI, 1976).

1.4. USE DATA

Dalapon is used in sugarcane, sugarbeets, corn, potatoes, asparagus, grapes, flax, new legume spring seedlings, citrus and deciduous fruit, coffee, certain stone fruits and nut trees for the control of annual and perennial grasses (WSSA, 1979). It can be applied with conventional aerial or ground equipment as a foliage application and applied prior to crop emergence or postemergence. Dalapon is applied at a rate of 0.75 lb/A in flax to 20 lb/A or more on noncropland; it is used with a water carrier at volumes of 5-300 gallons/acre, depending on crop situation, grass species and method of application and equipment available.

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. WATER

Hydrolysis of dalapon sodium salt proceeds by the following pathway which leads to the formation of pyruvic acid (Kenaga, 1974):

$$CH_3CCl_2CO_2 + Na^+ + H_2O \rightarrow CH_3COCO_2^- + H^+ + NaCl + HCl$$

Kenaga (1974) based this equation upon observations reported by Brust (1953) and Smith et al. (1957). Hydrolysis data for dalapon sodium salt are shown in Table 2-1; hydrolysis occurred slowly at 25°C at all concentrations. At 50°C, the rate of hydrolysis was more rapid, with ~25% hydrolysis occurring in 8 days at initial concentrations of 1, 5 and 18% in water. Hydrolysis of solutions of either dalapon or its sodium salt is accelerated at pH values >7 (Tacey and Bellinger, 1958). At 60°C, hydrolysis of dalapon sodium salt was 20% complete in 30 hours, at which time the equilibrium pH was 2.3. In contrast, 40% hydrolysis was seen in 40 hours when a pH of 12 was maintained during the hydrolysis. Considering all of the hydrolysis data discussed above, Kenaga (1974) has concluded that both dalapon salts and dalapon have chemical hydrolytic half-lives of several months at temperatures <25°C and solution concentrations of <1%. From an environmental viewpoint, chemical hydrolysis of dalapon does not appear to be a particularly significant degradation pathway when compared to degradation via micro-organisms in soil or water. Under most environmental conditions, microbial degradation of dalapon is virtually complete in 1 month (Kenaga, 1974).

Photolysis of aqueous solutions of dalapon has been studied by Tanaka (1972); however, irradiation was at 253.7 nm, and is of little use for environmental assessment purposes in the troposphere or on the earth. Since carboxylic acids show a forbidden $n \rightarrow \pi^*$ transition, generally <290 nm (absorption maxima), no significant photolysis of dalapon is expected.

TABLE 2-1

Hydrolysis of Dalapon[a]

Conditions of Hydrolysis		Hydrolysis (%)[b]		
Temperature (°C)	Time (hours)	Initial Concentration Dalapon Sodium Salt in Water		
		1%	5%	18%
25	102	0.27	0.43	0.53
	175	0.41	0.61	0.80
50	20	2.8	3.3	3.6
	95	16	15	17
100	1.5	53	48	45
	14.5	97	81	70

[a]Source: Brust, 1953

[b]Percent hydrolysis = $\frac{\text{moles chloride ion formed/2}}{\text{moles dalapon sodium salt}} \times 100$

Tindle et al. (1970) reported that 60% of radiolabeled dalapon (initial concentration, 1000 ppm) was converted to pyruvic acid after 1 month under normal laboratory lighting conditions; however, no dark controls were reported so that the effect of hydrolysis cannot be accounted for. Also, oxidation cannot be ruled out.

Data presented in Section 2.3. show that dalapon is readily degraded by micro-organisms. Alexander and Batchelder (1972) conducted BOD tests on dalapon sodium salt and Dowpon M (dalapon sodium plus magnesium salt) with microbial cultures obtained from an agricultural sandy loam, a city (Midland, MI) sewage sludge and a chemical waste sludge (Dow Chemical). Each microbial culture was acclimated at 70°F for 2 weeks with 20 ppm of each chemical. After acclimation, BOD tests were run on both the acclimated and the unacclimated cultures with Dowpon M and dalapon sodium salt, at 3.33 and 1.67 ppm, respectively; samples were incubated in the dark at 20°C. The acclimated cultures degraded the chemicals within 5 days, but the unacclimated cultures took longer (10-20 days). These data show the rapid biodegradation of dalapon sodium salt and Dowpon M with acclimated cultures (Kenaga, 1974). Foy (1961) found that a refrigerated water solution of dalapon became contaminated by micro-organisms. The changes that occurred in pure aqueous stock solution offered positive proof that some species of fungi, possibly Alternaria sp., are able to use dalapon as a sole carbon source (Kenaga, 1974).

Studies detailing the loss of dalapon from aquatic media by physical processes were not found in the literature cited in the Appendix. Since the K_a for dalapon is 2.94×10^{-2} and, consequently, 99+% of the dalapon in the environment may be dissociated, volatilization will not be a significant transport mechanism. Also, as noted in Section 2.3., dalapon is

readily leached in soils and has a very low soil adsorption coefficient. Therefore, dalapon sorption onto suspended particulate matter and subsequent sedimentation are unlikely to be significant.

Experimental BCFs for dalapon have been reported by Kenaga (1980a) and by Garten and Trabalka (1983). The BCFs in poultry, rodents, dogs and beef are all <1. The BCF in fish is 3 using the ecosystem test and 0.6 using the flowing water test. These values indicate that dalapon is not bioconcentrated to any significant extent.

The overall persistence of dalapon in aquatic media has not been studied extensively. An abstract of a Russian study (Buryi et al., 1971) reported that 3 days following the spraying of 30 kg dalapon/ha, the herbicide concentration in a stagnant 0.5 ha pond was 0.4 mg/ℓ and by day 10 had decreased to 0.15 mg/ℓ; in 10 ℓ jars the dalapon content decreased during a 40-day period from 5 to 0.25 mg/ℓ. It should be emphasized that the half-life of dalapon in aquatic media may vary, depending on the characteristics of the water body. Thus, the half-life may be different in pond, river and lake waters.

2.2. AIR

Specific data regarding the fate or transport of dalapon in the atmosphere were not located in the literature cited in the Appendix. Data summarized in Section 2.1. indicate that environmental photolysis is unlikely to occur and certainly is not a dominant process (i.e., within an order of magnitude of the fastest process). Also, Section 2.3. notes that dalapon is readily leached from soils and has a low soil adsorption coefficient. This indicates that sorption onto atmospheric particulate matter is not likely to be significant.

2.3. SOIL

The fate and transport of dalapon has been more adequately studied in soil than in atmospheric or aquatic media. Microbial degradation probably accounts for the major disappearance of this compound from soils.

Kenaga (1974) reviewed the available literature concerning the microbial degradation of dalapon by soil organisms. Thiegs (1955) found that the concentration of dalapon in previously sterilized (autoclaved) soil did not change, while a similar test with unsterilized soil containing micro-organisms caused the disappearance of dalapon in 4-5 weeks after one application and within 1 week after the second application of 50 ppm (indicating microbial adaptation). Jensen (1957) found that a group of bacteria (apparently Agrobacterium) decomposed dalapon, forming chloride ion in soil after an initial delay of 4 weeks; the delay was probably due to acclimation of the micro-organisms. Magee and Colmer (1969) found eight species of soil bacteria capable of decomposing dalapon. The organisms were capable of overcoming the inhibitory effect of dalapon when grown on agar at 5000 ppm; six of these species were tentatively identified as Agrobacterium and two as Pseudomonas. Hirsch and Alexander (1960) found that soil cultures of strains of Nocardia and Pseudomonas micro-organisms liberated 90-100% of the chlorine in dalapon in 3 weeks. Kaufman (1964) studied the microbial degradation of dalapon at 6 lb/A in five soils under greenhouse conditions and found that the rates of degradation depended on pH, organic matter, aeration and cation exchange capacity. By use of pure culture isolation of organisms adapted to dalapon sodium salt, Kearney et al. (1964) found that representatives of the following microbial genera were capable of liberating chloride ion from the dalapon ion: Pseudomonas, Agrobacterium, Bacillus, Alcaligenes, Arthrobacter and Nocardia. A cell-free preparation of an Arthrobacter sp.,

in a purified enzyme system, was found capable of dehalogenating dalapon to pyruvate. Beall et al. (1964) studied the comparative metabolism of 1-^{14}C- and 2-^{14}C-labeled dalapon by soil micro-organisms and pure cultures of Arthrobacter sp. Micro-organisms in muck soil degraded dalapon sodium salt in ~2 weeks; subsequent additions disappeared in ~2 days. Under anaerobic conditions with Arthrocater sp. using 2-^{14}C-labeled dalapon, pyruvate and an amino acid, alanine, were revealed as metabolic products. Corbin (1965) found that dalapon at 2000 ppm in soil containing Pseudomonas sp. was almost 100% detoxified within a 2-week period at 26°C and pH 6.5, and <50% detoxified at pH levels of 5.3 and 7.5 after 4 weeks, but not detectably detoxified at pH 4.3 after 8 weeks using a bioassay method. Burge (1969) determined the numbers of bacteria capable of decomposing dalapon sodium salt at 100 ppm in five soils by the most-probable-number method. Arthrobacter and Agrobacterium were found to increase readily on incubation with dalapon.

Berry et al. (1979) identified the bacterium Rhizobium as capable of utilizing dalapon as a sole source of carbon and energy. The release of chloride ions from the dalapon was found to result in the formation of pyruvate in cell-free extracts.

Specific data regarding hydrolysis or photolysis of dalapon in the soil were not found in the literature cited in the Appendix. As noted in Section 2.1., hydrolysis of dalapon in water media does not appear to be as significant a degradation factor as microbial degradation; however, the rates of hydrolysis in soils have not been investigated. Although data are not available, photolysis loss of dalapon from soil is probably insignificant when compared to microbial degradation.

The transport of dalapon from soil by leaching has been extensively investigated; WSSA (1979) has noted that dalapon readily leaches in soils. Helling (1971) conducted leaching tests on 40 pesticides based on Hagerstown silty clay loam; dalapon was determined to have an R_f value of 0.96, which classified it as very mobile. Kenaga (1980b) has calculated a soil adsorption coefficient (K_{oc}) for dalapon utilizing its water solubility; the K_{oc} for dalapon is 3. Soil adsorption coefficients below 100 are considered moderately to highly mobile. Warren (1954) determined the leachability of dalapon (sodium salt) in four soil types at 8 lb/A in comparison to other herbicides and found that dalapon moved readily in all four soil types. Holstun and Loomis (1956) studied the leaching of dalapon sodium salt at the rate of 24 lb a.i./A in glass soil-tube columns by the addition of 1.5 inches of water to the soil column; three silty loam and silty clay loam soils were modified by the addition of 10 and 20% sand or 4 or 8% manure. None of the soils adsorbed much dalapon; however, manure decreased and sand increased the downward mobility. Smith et al. (1972) studied the leaching of dalapon-^{14}C at the dosage of 1 lb/A through an 8.5-inch deep soil column of Kawkawlin sandy loam; 9 acre inches of water applied at 0.5-inch increments for wetting accounted for the leaching of 99.4% of the dalapon in the effluent of the soil column. Kas'yanenko and Cheremisina (1979) studied dalapon leaching in soil columns at a simulated rate of 40 kg dalapon/ha and 20-40 mm rain; the dalapon was completely leached from the top 6 cm of soil into the 18-20 cm deep soil. Popovich et al. (1982) tested the mobility of 18 pesticides in soil columns at doses equivalent to 5 kg/ha; dalapon remained in the 20 cm soil layer, while other pesticides migrated 20-80 cm deep.

The leaching tests described above were conducted under laboratory conditons. Miller and Getzandaner (1973) analyzed soils taken from various

locations in the United States under field conditions representing different climates, rainfall, soil types and soil depths. Samples were taken from a few days to 1 year after application of Dowpon M or Dowpon Grass Killer. Rates of application varied from 4-41 lb/A. No residues of dalapon were found in the 0-6 inch layer of soil from any treatment 40 days after application, and no residues of dalapon were found in the 6-12 inch layer of soil at any treatment rate or time interval from application. Kenaga (1974) has suggested that the above-mentioned study indicates that under many practical conditions dalapon does not leach more than 6 inches in soil, probably because microbial action proceeds at a significantly faster rate than leaching under favorable conditions. In an abstract of a foreign study, Boichev (1977) found that 3 weeks after application of 20 kg/ha of dalapon in April (10-21°C), the herbicide had leached from the topsoil and its content in the 30-60 cm deep soil layer was 0.04-0.05 ppm. Under low temperatures, dalapon was degraded slowly and penetrated to depths where it could contact grape roots. Dalapon applied in June at 22-23°C was degraded within 60-75 days. Eglite et al. (1979) studied the migration and residue in soil of dalapon applied in forests and tree nurseries in 1975-1977. Dalapon leaching was observed in forest soils at a depth of 40 cm; the highest concentrations were found at depths of 0-10 cm. In the soil, dalapon decomposed in 4-6 months.

The loss of dalapon through volatility from soil has not been investigated; however given that dalapon will be 99+% ionized under all environmentally relevant pHs, volatilization may not be a dominant process (i.e., it is not within an order of magnitude of the dominant process).

Finally, the persistence of dalapon as a result of all the microbial, chemical and physical processes has been widely. Some of the data already

presented in Chapter 2 has relevance to persistence measurements. WSSA (1979) have reported that the resultant average persistence at recommended rates of applications is 2-4 weeks in most agricultural soils during the growing season. Sengalevich et al. (1979) have reported the persistence of dalapon in Bulgarian soils to be 2-3 months. As noted earlier, the degradation rate of dalapon has some dependence upon pH, temperature, soil types and moisture content. Therefore, dalapon persistence will vary with geographic location and climatic conditions.

3. EXPOSURE

3.1. WATER

Very few monitoring data for dalapon exposure in the water environment were found in the literature searched (see Appendix). Frank et al. (1970) studied the concentrations of dalapon in irrigation water following canal bank applications of 6.7-20 lb/A. Maximum concentrations of dalapon found were 0.023- 0.365 ppm when sampled in the treated area within 30 minutes after application. The treated irrigation canals varied in water flow from 3.4-290 cu ft/sec and 0.96-2.4 ft/sec (2.4 ft/sec = 1.64 mph). After several hours, only very low levels of dalapon (<10 ppb) were present in waters flowing from the treated area. A concentration of 0.365 ppm dalapon in irrigation water would deposit only 0.09 lb of herbicide per acre-inch of water (Kenaga, 1974). The U.S. EPA data base STORET (see Appendix) does not have data for dalapon.

3.2. FOOD

Although dalapon is easily washed off of foliage, it is absorbed by both roots and leaves and translocates readily throughout the plant (WSSA, 1979). It accumulates in young tissue and may not be degraded (or only degraded very slowly) in certain plants (WSSA, 1979; Kenaga, 1974). However, specific data on the levels of dalapon residues in harvested crops were not located in the literature cited in the Appendix.

Garten and Trabalka (1983) have summarized the available bioaccumulation factors for dalapon in animals. The log bioaccumulation factors in poultry, rodents, dogs and cows are all negative, indicating virtually no bioaccumulation. For fish (static conditions), the log factor is 0.20, again indicating little bioaccumulation. Specific data on the levels of dalapon residues in animal food were not located in the literature.

3.3. INHALATION

Pertinant data regarding inhalation exposure to dalapon were not found in the literature cited in the Appendix.

3.4. DERMAL

Pertinent data regarding dalapon exposure to the skin were not found in the literature cited in the Appendix.

4. PHARMACOKINETICS

4.1. ABSORPTION

Hoerger (1969) demonstrated that dalapon is absorbed in humans following oral exposure. Volunteers were given five successive daily doses of 0.5 mg dalapon sodium salt/kg (198 mg/person). After 18 days ~50% of the administered dose was excreted in the urine.

Absorption of orally administered dalapon has also been observed in dogs (Hoerger, 1969; Paynter et al., 19609), rats (Paynter et al., 1960) guinea pigs, rabbits (Norris, 1969), cattle, pigs and sheep (Kenaga, 1974).

A single oral dose of 500 mg dalapon sodium salt/kg given to dogs was excreted (65-70% of the dose) in the urine within 2 days. Evidence of dalapon absorption in rats and dogs was provided by Paynter et al. (1960), who found residues of the herbicide in various tissues following long-term oral administration. Norris (1969) determined LD_{50}s for dalapon in guinea pigs and rabbits after oral administration. This indicates that absorption occurred.

4.2. DISTRIBUTION

Paynter et al. (1960) reported that rats fed diets containing 100 ppm dalapon sodium salt for 2 years had residue levels of 4.0 and 1.0 ppm in the kidney and liver, respectively. When fed diets containing 300 ppm for 2 years, the kidneys, liver, muscle, brain, fat and milk of rats contained 9.7, 3.5, 2.9, 2.6, 0.5 and 6.0 ppm dalapon, respectively. Similar administration of a diet containing 1000 ppm dalapon sodium salt resulted in kidney, liver, muscle, brain, fat and milk concentrations of 28.2, 10.7, 7.5, 5.4, 1.4 and 19.1, respectively. Dogs given 15 mg dalapon sodium salt/kg/day in capsular form for 1 year had herbicide residues in kidney, liver, muscle, brain and fat of 20, 22, 13, 9 and 1 ppm, respectively. Similar

administration of 50 mg dalapon sodium salt/kg/day resulted in kidney, liver, muscle, brain and fat residue levels of 26, 21, 20, 11 and 3 ppm, respectively. When the dosage level was increased 100 mg/kg/day, the kidney, liver, muscle, brain and fat contained 69, 52, 43, 21 and 10 ppm, respectively (Paynter et al., 1960).

4.3. METABOLISM

Rapid urinary excretion of unchanged dalapon occurs when the compound is fed to animals (Leasure, 1964). When radiolabeled ^{36}Cl-dalapon was fed to cows, only two radioactive compounds were observed in milk: unchanged dalapon and larger quantities of chloride ion. A pathway was postulated wherein dalapon undergoes hydrolysis to pyruvate, followed by further breakdown to acetate and carbon dioxide (Leasure, 1964).

4.4. EXCRETION

Dalapon is apparently not readily metabolized in animals, and, being highly water soluble, it is readily excreted in the urine (Kenaga, 1974). Dalapon is excreted in milk. When fed a diet containing 200 ppm dalapon sodium salt, cows produced milk containing 0.7-1.0 ppm of the herbicide for a period of about 8 weeks. Insignificant amounts of dalapon were found in milk fat or in the form of glyceride (Kenaga, 1974). Rats fed 300 and 1000 ppm dalapon sodium salt for 2 years produced milk containing 6.0 and 19.1 ppm of the herbicide, respectively (Paynter et al., 1960).

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of dalapon were not located in the available literature. Dalapon is currently scheduled for carcinogenicity testing by the National Toxicology Program (NTP, 1933).

A chronic study of the toxicity of dalapon sodium salt to rats is discussed in Section 5.5. (Paynter et al., 1960). The authors did not report the occurrence of any tumors.

5.2. MUTAGENICITY

The available data regarding the mutagenic potential by dalapon in micro-organisms indicates an absence of mutagenic effect (Table 5-1). The compound has been studied in Salmonella typhimurium, Escherichia coli, T_4 bacteriophage, Streptomyces coelicolor and Aspergillus nidulans. A positive result was observed in an in vivo assay in mice, but this Russian abstract reported few experimental details to that dalapon was (Kurinnyi et al., 1982).

5.3. TERATOGENICITY

Emerson et al. (1971) gave pregnant female rats 0, 500, 1000 or 1500 mg dalapon/kg/day in distilled water by gavage on days 6-15 of gestation. Day zero of gestation was considered to be the day on which sperm-positive vaginal smears were located. Dams were killed on day 20 of gestation; the fetuses were removed and weighed, and the number of viable fetuses, resorptions and corpora lutea were recorded. Fetuses were examined for external, skeletal and visceral abnormalities. Significant reductions in average weight of treated fetuses compared to controls were observed in the 1000 and 1500 mg dalapon/kg/day treatment groups, but not at the lower doses. No other dose-related abnormalities were observed in dalapon-treated fetuses.

TABLE 5-1

Mutagenicity Data for Dalapon

Assay	Indicator Organism	Compound	Concentration	Application	Metabolic Activation	Response*	Comment	Reference
Reverse mutation	Salmonella typhimurium	dalapon sodium salt (85%)	"small crystals"	agar overlay	none	-	NC	Andersen et al., 1972
Reverse mutation	S. typhimurium TA1535, TA1536, TA1537, TA1538	dalapon	NR	plate incorporation	none	-	NC	Carere et al., 1976
Reverse mutation	S. typhimurium TA98, TA100, TA1535, TA1537, TA1538	dalapon	<5 mg/plate	plate incorporation	+ rat liver S-9	-	NC	Moriya et al., 1983
Reverse mutation	Escherichia coli WP2 hcr	dalapon	<5 mg/plate	plate incorporation	+ rat liver S-9	-	NC	Moriya et al., 1983
Reverse mutation	T_4 bacteriophage AP72, E. coli KB,B	dalapon sodium salt (85%)	500 µg	liquid holding	none	-	NC	Andersen et al., 1972
Reverse mutation	T_4 bacteriophage N17, E. coli KB, B	dalapon sodium salt	25 µg	liquid holding	none	-	NC	Andersen et al., 1972
Induction of streptomycin resistance	Streptomyces coelicolor	dalapon	NR	plate incorporation	none	-	NC	Carere et al., 1976
Mitotic nondisjunction	Aspergillus nidulans	dalapon sodium salt	<800 µg/ml	plate incorporation	none	-	NC	Morpurgo et al., 1979
Chromosome aberration	mouse (strain NR) bone marrow	dalapon	NR	in vivo	NA	+	increased number of metaphases with chromosome aberrations	Kurinnyi et al., 1982

*Responses: +, positive; -, negative; =, negative with and without S9 activation system; ±, positive with and negative without S9 activation system; ±, negative with and positive without S9 activation system

NA = Not available

NC = No comment

NR = Not reported

In a range-finding study, Thompson et al. (1971) gave pregnant rats 250, 500, 1000, 1500 or 2000 mg dalapon/kg/day by gavage on days 6-15 of gestation. Maternal and fetal body weight, food consumption, number of viable fetuses, fetal resorptions, corpora lutea and gross observations were recorded. Evidence of maternal toxicity (diarrhea and reduced weight gain) was observed in the 1500 and 2000 mg dalapon/kg/day treatment groups. Significantly decreased weights of treated fetuses compared to controls were observed in the 2000 mg dalapon/kg/day treatment group. No effects were observed in the 1000, 500 or 250 mg dalapon/kg/day treatment groups that were different from those of controls.

5.4. OTHER REPRODUCTIVE EFFECTS

Paynter et al. (1960) conducted a three-generation reproduction study on albino rats exposed to dalapon sodium salt in their diets. Groups of 4 male and 12 female young albino rats were maintained for 110 days on diets containing 0, 0.03, 0.1 or 0.3% dalapon sodium salt. These groups were allowed to mate and bear young. Litters were culled to eight pups until weaning. When weaned groups of the young rats (4 male and 12 female) were maintained on similar diets for 110 days and allowed to mate and bear young. The procedure was conducted for a third generation. A total of 261 litters were observed. No adverse effects were reported. The indices of reproductive toxicity evaluated were fertility, gestation, litter size, viability, lactation and body weight.

5.5. CHRONIC AND SUBCHRONIC TOXICITY

Paynter et al. (1960) maintained groups of 10 male and 10 female young Wistar-Dow rats on diets containing 0, 0.0115, 0.0346, 0.115, 0.346 or 1.15% of a commercial grade of dalapon for 97 days. These levels are equivalent to dosages of 0, 11.5, 34.6, 115, 346 or 1115 mg dalapon sodium salt/kg/day,

assuming that young, growing rats consume food at a rate of 10% of their body weight/day. Body weights, food consumption, mortality and hematological indices were recorded during exposure, and histopathological examination was performed after exposure ceased. No effect was observed in male rats ingesting <115 mg dalapon sodium/kg/day or females ingesting 11.5 mg dalapon sodium/kg/day. Statistically significant increases in average kidney weights were observed in females ingesting 34.6 and 115 mg dalapon sodium salt/kg/day. At the higher doses (346 and 1115 mg dalapon sodium salt/kg/day), no adverse effects on mortality, food consumption or blood, lung, heart and spleen histopathology were observed. Growth retardation, increased liver and kidney weights and slight renal and hepatic histopathological changes were observed at the two highest dose levels (346 and 1115 mg dalapon sodium salt/kg/day).

Paynter et al. (1960) gave groups of two male and one female mongrel dogs capsules containing 0, 15, 50 or 100 mg commercial dalapon sodium salt/kg/day 5 days/week for 52 weeks. The animals were observed for signs of toxicity; body weight and daily food consumption were recorded weekly. Urinalysis, bromosulfalein liver function tests, blood chemistry determinations and blood counts were made on each dog initially and at the end of the 13th, 26th and 52nd weeks. At the end of exposure, all dogs were killed, and gross autopsies and histopathological examinations were performed. No abnormal behavior or reactions to dalapon treatment were observed. No significant effects of treatment were observed when compared to controls for blood chemistry, urinalysis or organ-to-body weight ratios for the lungs, heart, liver, spleen or testes at any dose level. A statistically significant increase over controls was observed in the average kidney-to-body

weight ratio in dogs receiving 100 mg dalapon sodium/kg/day. No treatment-related histopathologic effects were seen in the kidneys or other organs.

Paynter et al. (1960) maintained groups of 24 male and 20 female Albino Carworth Farm rats on diets providing 0, 5, 15 or 50 mg commercial dalapon sodium salt/kg/bw/day for 2 years. Blood counts and hemoglobin determinations were conducted on at least two males and two females from each dosage group at 0, 26, 52 and 104 weeks. Animals (2/sex/group) were killed after 26 weeks and two males/group were killed after 52 weeks for gross and histopathologic examination. The surviving rats were killed at 104 weeks, at which time gross autopsies and organ weight determinations were made on all animals; histopathologic examinations were performed on "representative male and female animals from each group." A statistically significant ($p<0.05$) increase over controls was observed in the kidney-tobody weight ratios of male rats receiving 50 mg dalapon sodium salt/kg/day. No differences from controls were observed in any treatment groups on any of the other criteria evaluated, including the histopathologic examination of the kidneys.

5.6. OTHER RELEVANT INFORMATION

Dalapon may be irritating to the eyes, skin and respiratory tract (WSSA, 1979). When powdered dalapon was placed in the eye of a rabbit, indications of immediate pain and irritation were observed. Cornea injury and conjunctivitis were observed 1 hour after application. When a 10% aqueous solution of dalapon was placed in rabbits' eyes, slight pain, conjunctivitis were observed. No reaction was observed when a 1% solution was applied. Similar results were observed with dermal application of dalapon. Necrosis and hyperemia were observed when undiluted dalapon was applied to shaved rabbit

skin. When 10 and 1% aqueous solutions of dalapon were applied, the investigators observed slight and no irritation, respectively (Paynter et al., 1960).

The LD_{50}s of dalapon in mammals have been observed to exceed 3860 mg/kg, reflecting a low order of acute toxicity.

Less than 1% of the dalapon included in the feed of cows was detected in their milk. When ^{36}Cl-dalapon supplemented feed was used, the milk was observed to contain unchanged dalapon and chloride ion (Leasure, 1964).

Dalapon has been reported to activate pyruvate dehydrogenase in pig and rat heart tissue (Whitehouse et al., 1974) and to inhibit urease activity in vitro (Olson and Christensen, 1982).

6. AQUATIC TOXICITY

6.1. ACUTE EFFECTS

Data on the lethal effects of acute exposure to dalapon in freshwater fish (Table 6-1) and aquatic invertebrates (Table 6-2) are abundant. Dalapon has been regarded as having a low aquatic toxicity, but lethal levels range from 44 mg/ℓ (48 hours exposure in soft water) for harlequin fish, R. heteromorpha (Alabaster, 1969), to >30,000 mg/ℓ in carp (96-hour exposure) (Spehar et al., 1981). Water hardness and the method of study, either static or flow through systems, have been shown to affect toxicity to a notable degree. For example, the 24- and 48-hour LC_{50}s for dalapon in the harlequin fish were both >500 mg/ℓ in hard water (250 mg $CaCO_3$/ℓ) and 49 and 44 mg/ℓ, respectively, in soft water (20 mg $CaCO_3$/ℓ) (Alabaster, 1969). In largemouth bass, Micropterus salmoides, the 48-hour LC_{50} in static conditions was >1000 mg dalapon/ℓ, while in a flow-through system 100% mortality occurred at this concentration (McKee and Wolf, 1963). In three common sport fish, coho salmon, rainbow trout and bluegill sunfish, LC_{50} values for dalapon were 340 (48-hour value), 340 (96-hour) and 105 (96-hour) mg/ℓ, respectively (Folmar, 1976; McKee and Wolf, 1963; Cope, 1965).

Several species of crustaceans and aquatic invertebrates have been tested for susceptiblity to dalapon (see Table 6-2). The brown shrimp and species of water fleas, important fish-food organisms, appear to be quite sensitive, having median lethality levels near or below 16 mg dalapon/ℓ (Butler, 1965; Sanders and Cope, 1966; U.S. NTACWQC, 1968). The oyster, Crassostrea virginica, showed no toxic effects at 1.0 mg dalapon/ℓ (Butler, 1965).

TABLE 6-1

Acute Letnal Effects of Dalapon to Freshwater Fish

Species	Duration (hours)	Concentration (mg/ℓ)	Method	Effect	Reference
Coho salmon, *Oncorhynchus kisutch*	48	340	static; aerated	LC_{50}	McKee and Wolf, 1963
Rainbow trout, *Salmo gairdneri*	96	340	NR	LC_{50}	Folmar, 1976
Bluegill sunfish, *Lepomis macrochirus*	24	115	static	LC_{50}	Cope, 1965
	48	115	static	LC_{50}	
	96	105	static	LC_{50}	
Bluegill sunfish, *Lepomis macrochirus*	24	480	NR	LC_{50}	Surber and Pickering, 1962
	96	290	NR	LC_{50}	
Largemouth bass, *Micropterus salmoides*	48	>1000	static; aerated	LC_{50}	McKee and Wolf, 1963
	48	1000	flow through	100% mortality	
	168	250	flow through	no mortality	
Fathead minnow, *Pimephales promelas*	24	440	NR	LC_{50}	Surber and Pickering, 1962
	96	290	NR	LC_{50}	
Red-sided shiner, *Richardsonius balteatus*	96	390	aerated; hard water	LC_{50}	McKee and Wolf, 1963
	96	395	aerated; soft water	LC_{50}	
Emerald shiner, *Notropis atherinoides*	72	3000	NR	no mortality	McKee and Wolf, 1963
	72	5000	NR	100% mortality	
Channel catfish, *Ictalurus punctatus*	48	10	static	<10% mortality	McCorkle et al., 1977

TABLE 6-1 (cont.)

Species	Duration (hours)	Concentration (mg/ℓ)	Method	Effect	Reference
Carp, *Ctenopharyngodon idella*	96	>30,000	static	LC_{50}	Spehar et al., 1981
Guppy, *Paecilia reticulata*	96	223	static	LC_{50}	Kam-Wing and Furtado, 1977
Mosquitofish, *Gambusia affinis*	96	19,000	static	LC_{50}	Johnson, 1978
Harlequin fish, *Rasbora heteromorpha*	24	>500	static; hard water	LC_{50}	Alabaster, 1969
	24	49	static; soft water	LC_{50}	
	48	>500	static; hard water	LC_{50}	
	48	44	static; soft water	LC_{50}	
Harlequin fish, *Rasbora trilineata*	96	135	static	LC_{50}	Kam-Wing and Furtado, 1977
Bleak, *Alburnus alburnus*	96	5,500	static	LC_{50}	Linden et al., 1979
Heteropneustes fossils	192	2,500	NR	no mortality	Rao and Dad, 1979
Sarotherodon massambicus	192	2,500	NR	no mortality	Rao and Dad, 1979
Punctius ticto	192	2,500	NR	no mortality	Rao and Dad, 1979

NR = Not reported

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TABLE 6-2

Acute Lethal Effects of Dalapon in Aquatic Invertebrates

Species	Duration (hours)	Concentration (mg/ℓ)	Method	Effect	Reference
Brown shrimp, *Penaeus aztecus*	24 48	1.0 1.0	static static	30% mortality 40% mortality	Butler, 1965
Water flea, *Daphnia magna*	48	6	static	LC_{50}	U.S. NTACWQC, 1968
Water flea, *Daphnia pulex*	48	11	static	LC_{50}	Sanders and Cope, 1966
Water flea, *Simocephalus serrulatus*	46	16	static	LC_{50}	Sanders and Cope, 1966
Copepod, *Nitocra spinipes*	96	4800	static	LC_{50}	Linden et al., 1979
Stonefly, *Pteronarcys californica*	96 96	100 >1000	static static	no effect LC_{50}	Sanders and Cope, 1968
Oyster, *Crassostrea virginica*	96	1.0	static	no effect on shell growth	Butler, 1965

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6.2. CHRONIC EFFECTS

Alabaster (1969) estimated that the mean threshold concentration for 50% mortality during a 3-month exposure to dalapon would be ~40 mg/ℓ in the harlequin fish. This estimation was based on acute testing in soft water conditions.

In a study exposing the Indian fish, Heliodiaptomus viduus, to dalapon at 0.1, 1.0, 10 and 100 mg/ℓ for up to 33 days, increased exposure levels were associated with extended survival (George et al., 1982). The LT_{50}s for exposure at 0.1, 1.0, 10 and 100 mg/ℓ were 315, 333, 193 and 461 hours, respectively. The corresponding times for 100% mortality were 648, 348, 768 and 792 hours for exposure levels, respectively. An explanation for this occurrence was not discussed.

In a German study, available in an English abstract, Schulz (1981) reported that carp, Cyprinus carpio, exposed to 2.5 mg dalapon/ℓ (for possibly up to 63 days) had decreased appetites, altered behavior and decreased RNA and ribosomes in the exocrine pancreas.

6.3. PLANT EFFECTS

Dalapon is used as a herbicide to control aquatic plant growth and is usually applied at ~20 lb/A (Battelle Columbus Laboratories, 1971). Application of ~15 lb/A (1 lb/7.5 gal) effectively controlled the growth of cattails and other aquatic plants. Johannes (1967) reported that dalapon was one of the "safest herbicides for submerged weeds in pond tests" when applied at 20 lb/ha and reached safe residual levels within ~1 week.

Dalapon at 1 mg/ℓ was not effective in decreasing the productivity of a mixed population of phytoplankton following a 4-hour exposure (FWS, 1964).

6.4. RESIDUES

Pertinent data regarding the persistence of dalapon residues in fish or aquatic organisms were not located in the literature cited in the Appendix.

6.5. OTHER RELEVANT INFORMATION

The ability of rainbow trout, Salmo gairdneri, to detect and avoid dalapon-contaminated water was tested by Folmar (1976). Fish exposed to flowing channels of contaminated and uncontaminated water consistently avoided dalapon at 1.0 and 10.0 mg/ℓ in a dose-related manner. At 1.0 mg/ℓ, 82% of the fish were located in dalapon-free water, while at 10.0 mg/ℓ 96% of the fish avoided the contaminated channel.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

The American Conference of Governmental Industrial Hygienists (ACGIH, 1980) has adopted a TLV for occupational exposure to dalapon of 1 ppm (6 mg/m^3) for an 8-hour TWA exposure.

A tolerance of 0.2 ppm was established for dalapon in potable water, resulting from its application to irrigation ditch banks (CFR, 1983). Tolerances for dalapon residues have been established for a variety of agricultural commodities; these range from 0.1 ppm in milk, sugar cane and pecans to 75 ppm on flax seed (CFR, 1978).

7.2. AQUATIC

Under FIFRA (Federal Insecticide, Fungicide and Rodenticide Act) an acceptable pesticide residue level for dalapon in drinking water is determined as 0.2 ppm (Federal Register, 1983).

8. RISK ASSESSMENT

Data demonstrative of the carcinogenicity, mutagenicity and teratogenicity of dalapon were not located in the literature cited in the Appendix.

The subchronic and chronic feeding studies in rats and dogs reported by Paynter et al. (1960) may provide a basis for assessing the human health risks of dalapon exposure. In small groups of dogs (3/group) given dalapon sodium by capsule for 1 year, a LOEL and a NOEL were found at doses of 100 mg dalapon sodium/kg/day and 50 mg dalapon sodium/kg/day, respectively. The most sensitive effect observed was an increase in the average kidney-to-body weight. Rats appear to be a more sensitive species. When fed 50 mg dalapon sodium/kg/day for 2 years, male rats experienced increased kidney-to-body weight. This dose level can be considered a chronic LOEL. The chronic NOEL in rats was at a dose of 15 mg dalapon sodium/kg/day. These levels were supported by a 97-day subchronic feeding study in rats in which female rats had a subchronic NOEL at 11.5 mg dalapon sodium/kg/day and a subchronic LOEL at 34.6 mg dalapon sodium salt/kg/day. An effect similar to that in the chronic study, increased kidney-to-body weight, was observed in rats fed $\geq$34.6 mg dalapon sodium/kg/day.

An ADI for humans can be calculated from the chronic NOEL in rats of 15 mg dalapon sodium/kg/day (Paynter et al., 1960). The authors stated that the material used in this study, called dalapon sodium, contained 65% of 2,2-dichloropropionic acid sodium salt. The dosage of dalapon (2,2-dichloropropionic acid) found to cause no effect is equivalent to 8.45 mg dalapon/kg/day. This is obtained by multiplying the NOEL dose by the percentage of dalapon and the ratio of the molecular weights of dalapon and its sodium salt [15 mg x 0.65 x (143/165)]. A human ADI of 0.0845 mg/kg/day for dalapon is thus obtained by dividing 8.45 by an uncertainty factor of 100.

This factor is appropriate because a factor of 10 is applied to extrapolate from a chronic animal NOEL to humans, and an additional factor of 10 is applied to protect the most sensitive humans.

Statements concerning available literature in this document refer to published, quotable sources and are in no way meant to imply that confidential data, which this document could not address, are not in existence. These data, which are considered Confidential Business Information (CBI), are available in summary form as a CBI Appendix that can be accessed by individuals with appropriate clearance. Conclusions from the CBI Appendix regarding risk assessment can, however, be presented in this chapter.

The CBI Appendix to this document reviews other animal studies, but the data do not necessitate a change in the above risk assessment.

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APPENDIX:

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE

These searches were conducted in November, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7th), and the following secondary sources were reviewed:

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